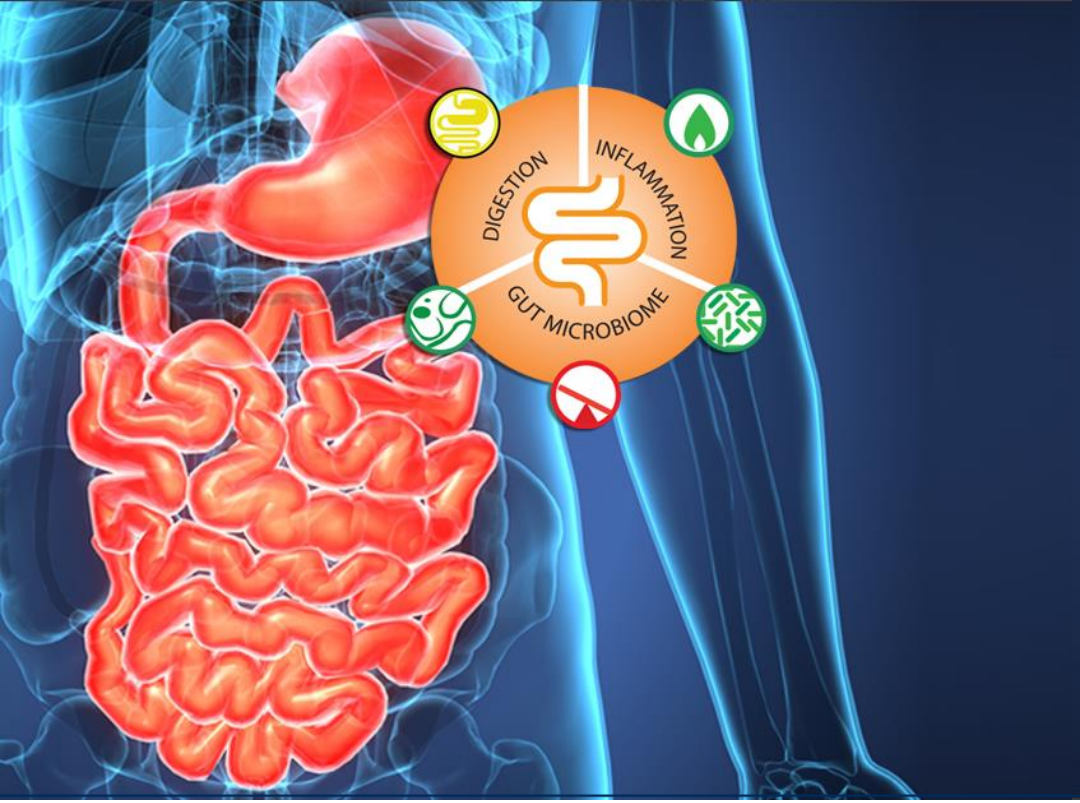


GI effects®

The GI Effects Comprehensive Report Review: A Global Evaluation of GI Function

Stephen L. Goldman, DC
Genova Diagnostics

GENOVA DIAGNOSTICS®

Stephen L. Goldman, DC

Medical Education Specialist

GENOVA DIAGNOSTICS®

Methodology: Vitek 2® System Microbial Antibiotic susceptibility, Manual Minimum Inhibition Concentration

Mycology Sensitivity

Candida Susceptibility Profile for Azoles*

Organism	Number of Isolates	% Sensitive	
		Fluconazole	Voriconazole
Candida albicans	25561	99.19%	99.51%
Candida parapsilosis	8777	98.64%	99.33%
Candida kruseii	3420	0.23%	97.79%
Candida tropicalis	1076	93.22%	90.57%
Candida glabrata	2898	27.1%	90.9%

***Results of pharmaceutical sensitivities against certain yeast species are based on internal Genova data pertaining to the frequency of susceptibility of the specific yeast to the listed antifungal agent. The pharmaceutical results are not patient-specific. Conversely, the results of inhibition to nystatin and natural agents are patient-specific.**

Non-absorbed Antifungals

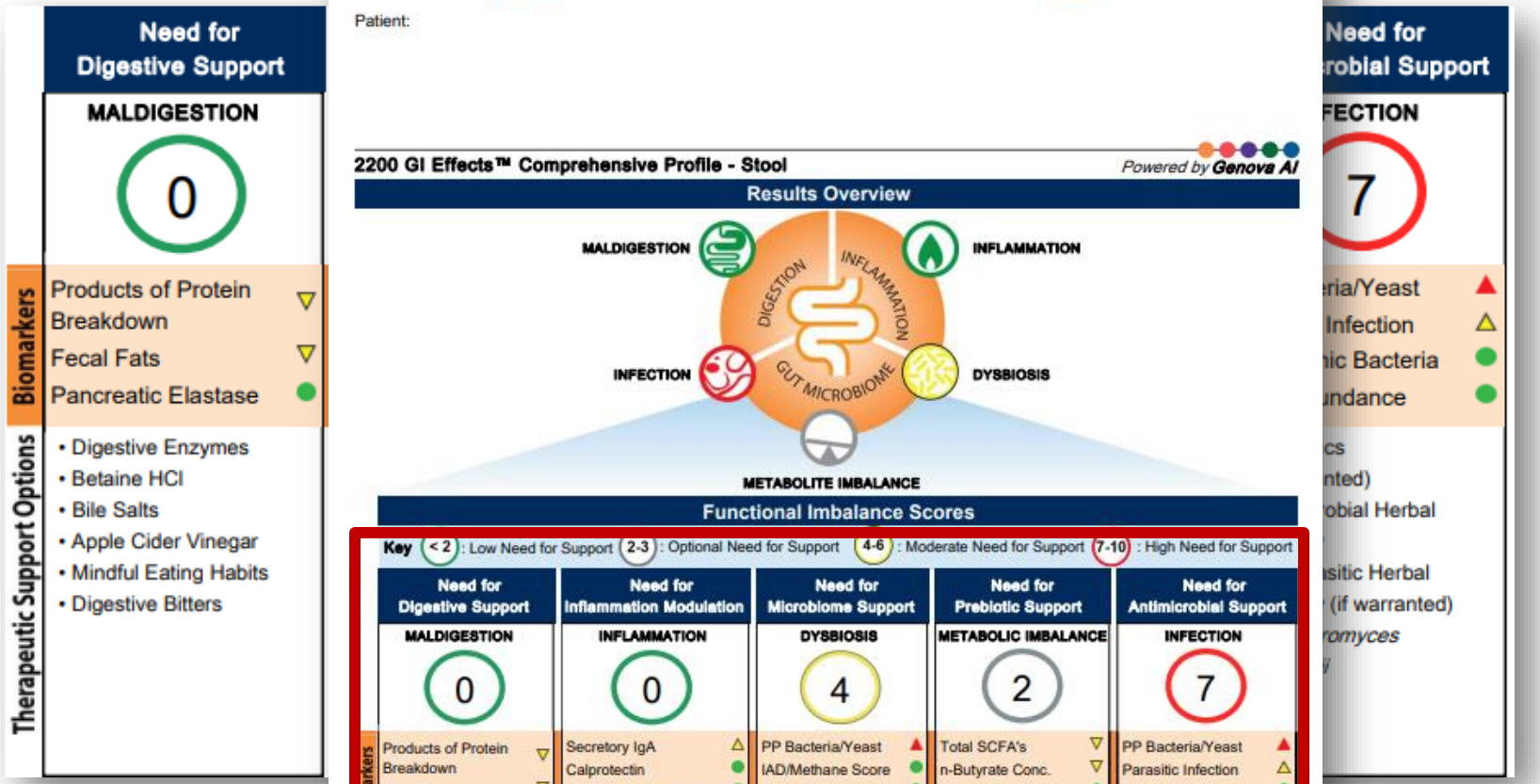
Candida kruseii	LOW INHIBITION	HIGH INHIBITION
Nystatin		

Natural Agents

Candida kruseii	LOW INHIBITION	HIGH INHIBITION
Berberine		
Caprylic Acid		
Garlic		
Undecylenic Acid		
Uva-Ursi		

Nystatin and Natural Agents:
Results for Nystatin are being reported with natural antifungals in this category in accordance with laboratory guidelines for reporting sensitivities. In this assay, inhibition is defined as the reduction level on organism growth as a direct result of inhibition by a natural substance. The level of inhibition is an indicator of how effective the substance was at limiting the growth of an organism in an in vitro environment. High inhibition indicates a greater ability by the substance to limit growth, while Low Inhibition a lesser ability to limit growth. The designated natural products should be considered investigational in nature and not be viewed as standard clinical treatment substances.

Therapeutic Su



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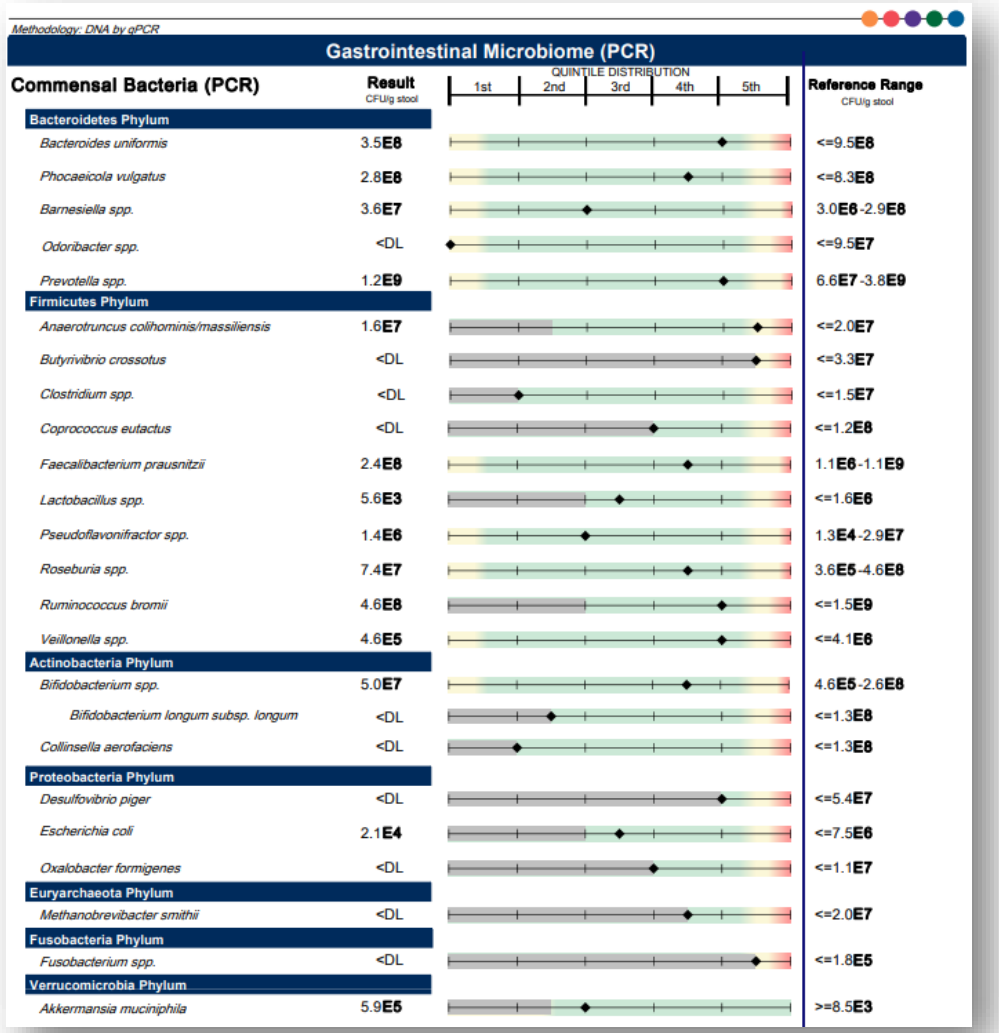
ons left up to clinician

GENOVA DIAGNOSTICS

Commensal Bacteria



Methodology: DNA by qPCR

Gastrointestinal Microbiome (PCR)

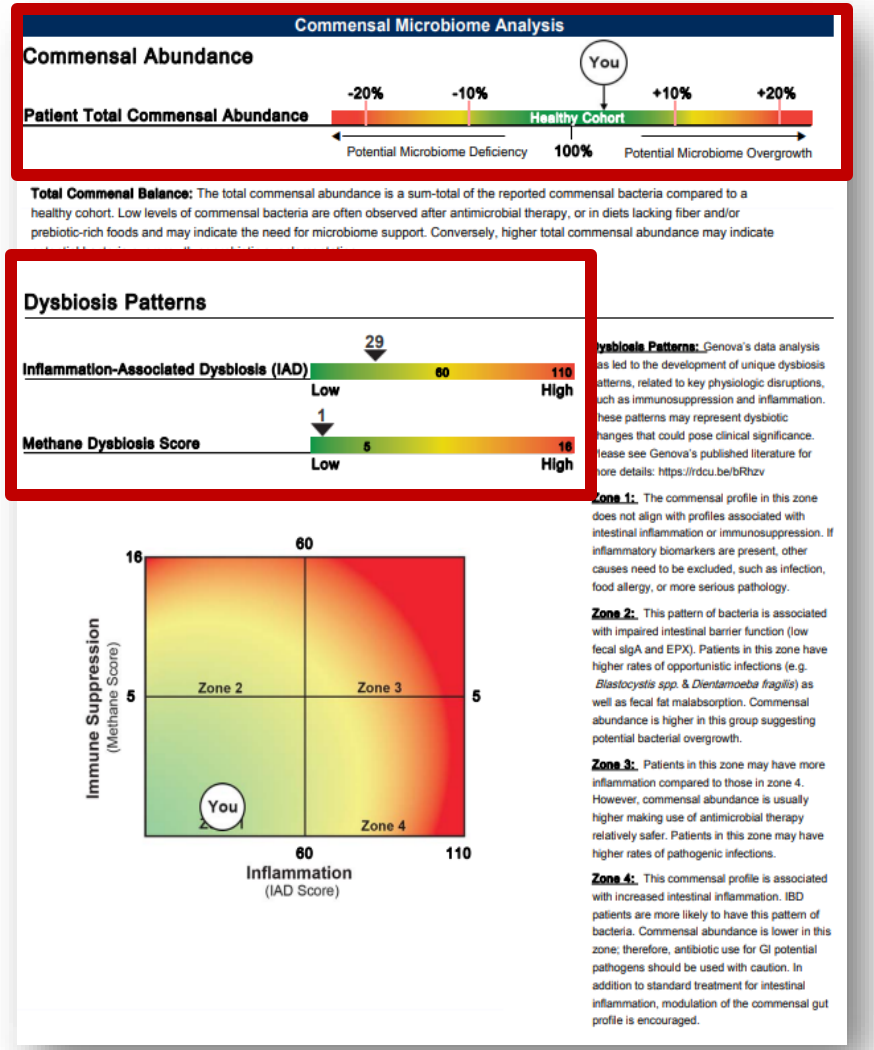
Commensal Bacteria (PCR)	Result (CFU/g stool)	Quintile Distribution (1st–5th)	Reference Range (CFU/g stool)
Bacteroidetes Phylum			
Bacteroides uniformis	3.5E8		<=9.5E8
Phocaeicola vulgatus	2.8E8		<=8.3E8
Barnesiella spp.	3.6E7		3.0E6-2.9E8
Odoribacter spp.	<DL		<=9.5E7
Prevotella spp.	1.2E9		6.6E7-3.8E9
Firmicutes Phylum			
Anaerotruncus colihominis/massiliensis	1.6E7		<=2.0E7
Butyrivibrio crossotus	<DL		<=3.3E7
Clostridium spp.	<DL		<=1.5E7
Coprococcus eutactus	<DL		<=1.2E8
Faecalibacterium prausnitzii	2.4E8		1.1E6-1.1E9
Lactobacillus spp.	5.6E3		<=1.6E6
Pseudoflavonifractor spp.	1.4E6		1.3E4-2.9E7
Roseburia spp.	7.4E7		3.6E5-4.6E8
Ruminococcus bromii	4.6E8		<=1.5E9
Veillonella spp.	4.6E5		<=4.1E6
Actinobacteria Phylum			
Bifidobacterium spp.	5.0E7		4.6E5-2.6E8
Bifidobacterium longum subsp. longum	<DL		<=1.3E8
Collinsella aerofaciens	<DL		<=1.3E8
Proteobacteria Phylum			
Desulfovibrio piger	<DL		<=5.4E7
Escherichia coli	2.1E4		<=7.5E6
Oxalobacter formigenes	<DL		<=1.1E7
Euryarchaeota Phylum			
Methanobrevibacter smithii	<DL		<=2.0E7
Fusobacteria Phylum			
Fusobacterium spp.	<DL		<=1.8E5
Verrucomicrobia Phylum			
Akkermansia muciniphila	5.9E5		>=8.5E3

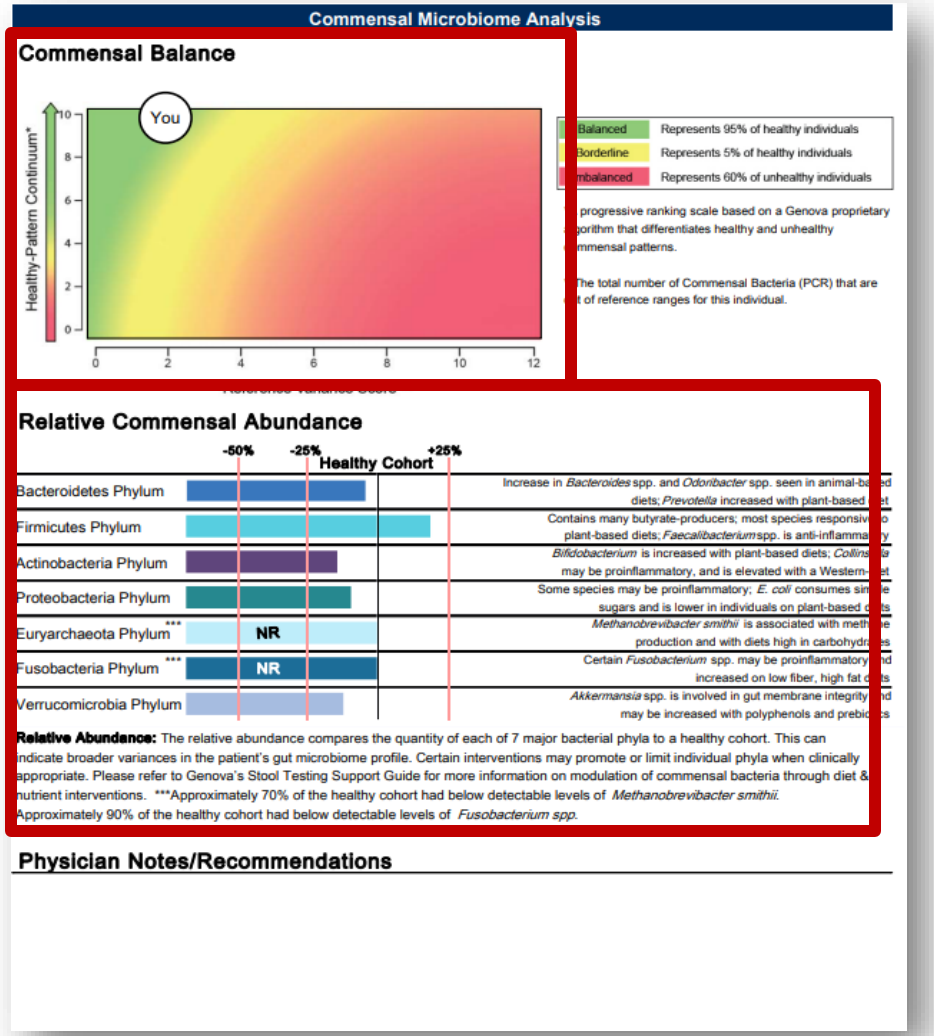
- Clinicians often struggle with what to do with DNA PCR analysis of commensal bacteria
- Historical limitations
  - Methodologies differ in literature
  - Discrepant results in publications
  - Unknown clinical importance of individual bacteria
  - No research into bacterial patterns

GENOVA DIAGNOSTICS

A Novel Approach to Microbiome Analysis

1. *Abundance*
2. *Patterns*
3. *Balance*

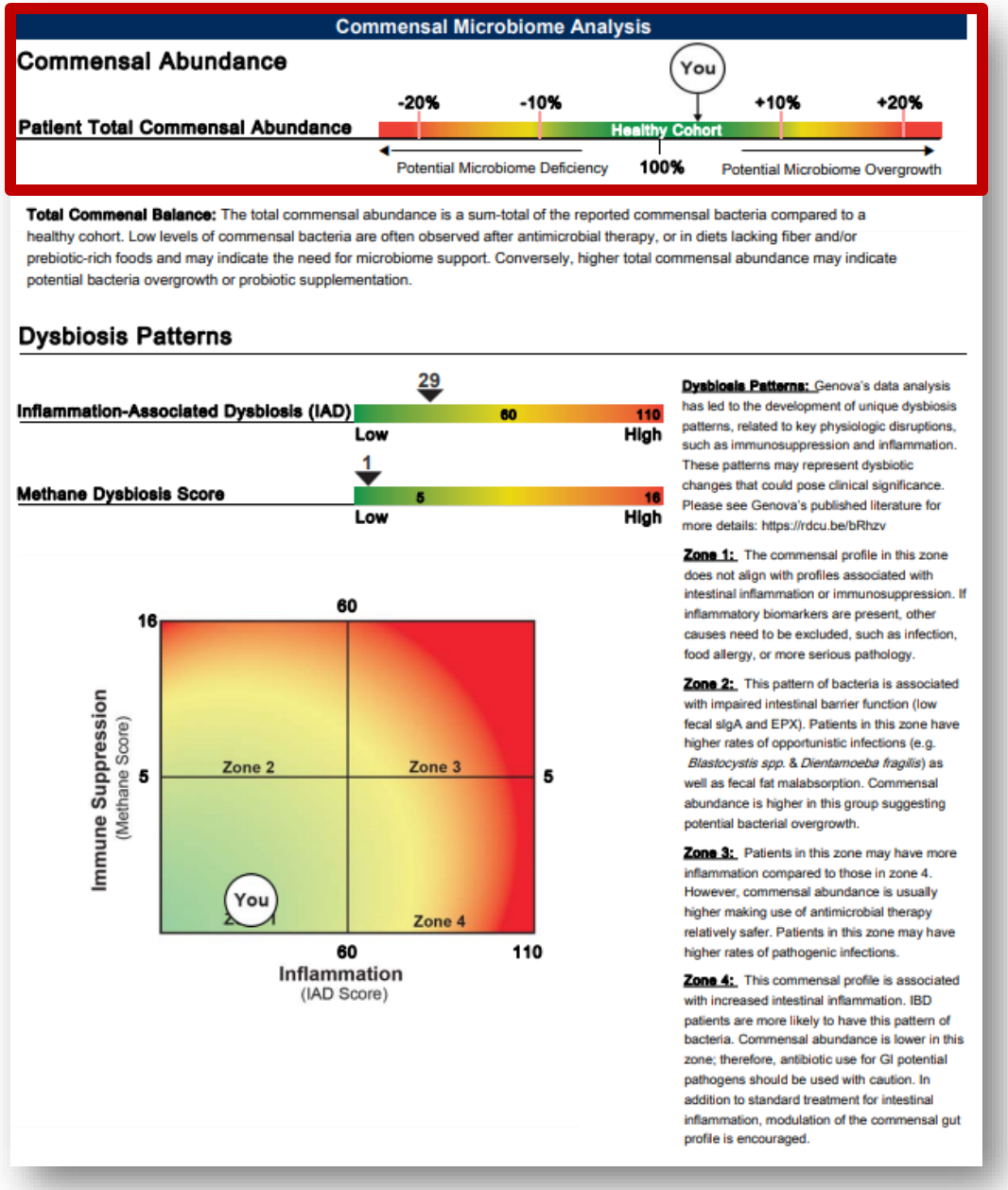




GENOVA DIAGNOSTICS

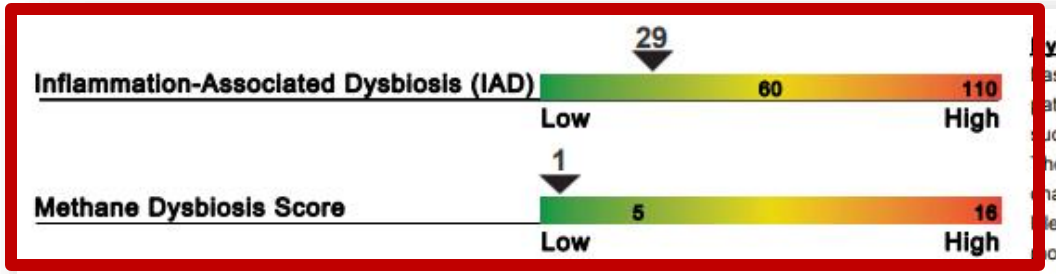
Commensal Abundance

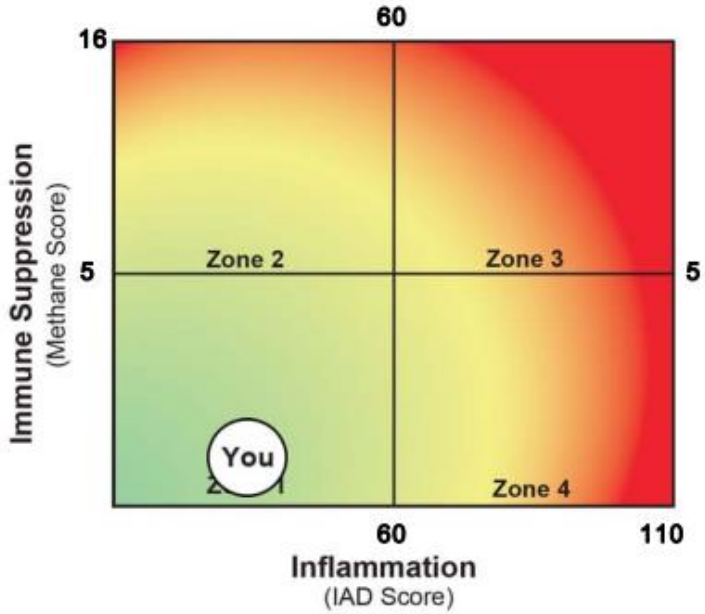
- **Shift-to-the-Right**: Patient has more overall commensal bacteria
  - May be indicative of potential microbial overgrowth, such as in small intestinal bacterial overgrowth (SIBO)
  - May also be due to recent supplementation with probiotics
- **Shift-to-the-Left**: Patient has less overall commensal bacteria
  - May be indicative of potential microbiome deficiency, such as following antibiotic use
  - May indicate a diet low in fiber and prebiotic foods



GENOVA DIAGNOSTICS

Dysbiosis Patterns





Dysbiosis Patterns: Genova's data analysis has led to the development of unique dysbiosis patterns, related to key physiologic disruptions, such as immunosuppression and inflammation. These patterns may represent dysbiotic changes that could pose clinical significance. Please see Genova's published literature for more details: https://rdcu.be/bRhzv

Zone 1: The commensal profile in this zone does not align with profiles associated with intestinal inflammation or immunosuppression. If inflammatory biomarkers are present, other causes need to be excluded, such as infection, food allergy, or more serious pathology.

Zone 2: This pattern of bacteria is associated with impaired intestinal barrier function (low fecal sIgA and EPX). Patients in this zone have higher rates of opportunistic infections (e.g. *Blastocystis spp.* & *Dientamoeba fragilis*) as well as fecal fat malabsorption. Commensal abundance is higher in this group suggesting potential bacterial overgrowth.

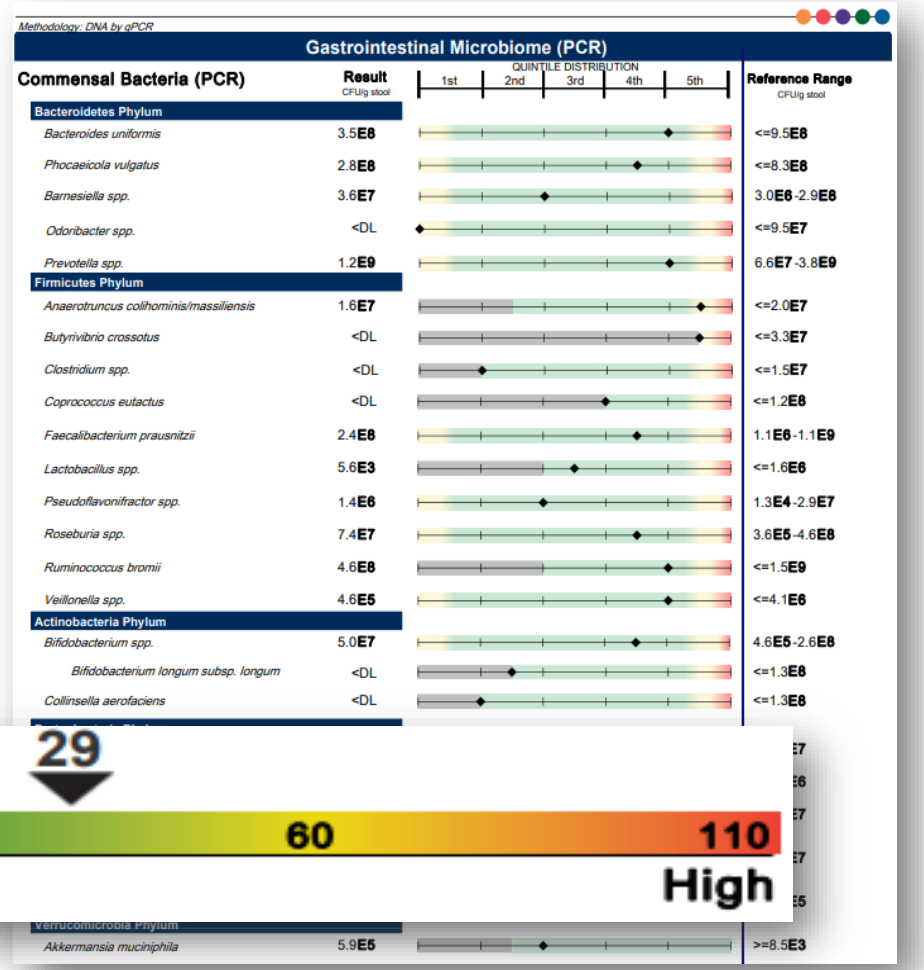
Zone 3: Patients in this zone may have more inflammation compared to those in zone 4. However, commensal abundance is usually higher making use of antimicrobial therapy relatively safer. Patients in this zone may have higher rates of pathogenic infections.

Zone 4: This commensal profile is associated with increased intestinal inflammation. IBD patients are more likely to have this pattern of bacteria. Commensal abundance is lower in this zone; therefore, antibiotic use for GI potential pathogens should be used with caution. In addition to standard treatment for intestinal inflammation, modulation of the commensal gut profile is encouraged.

GENOVA DIAGNOSTICS

Inflammation-Associated Dysbiosis Score (IAD)

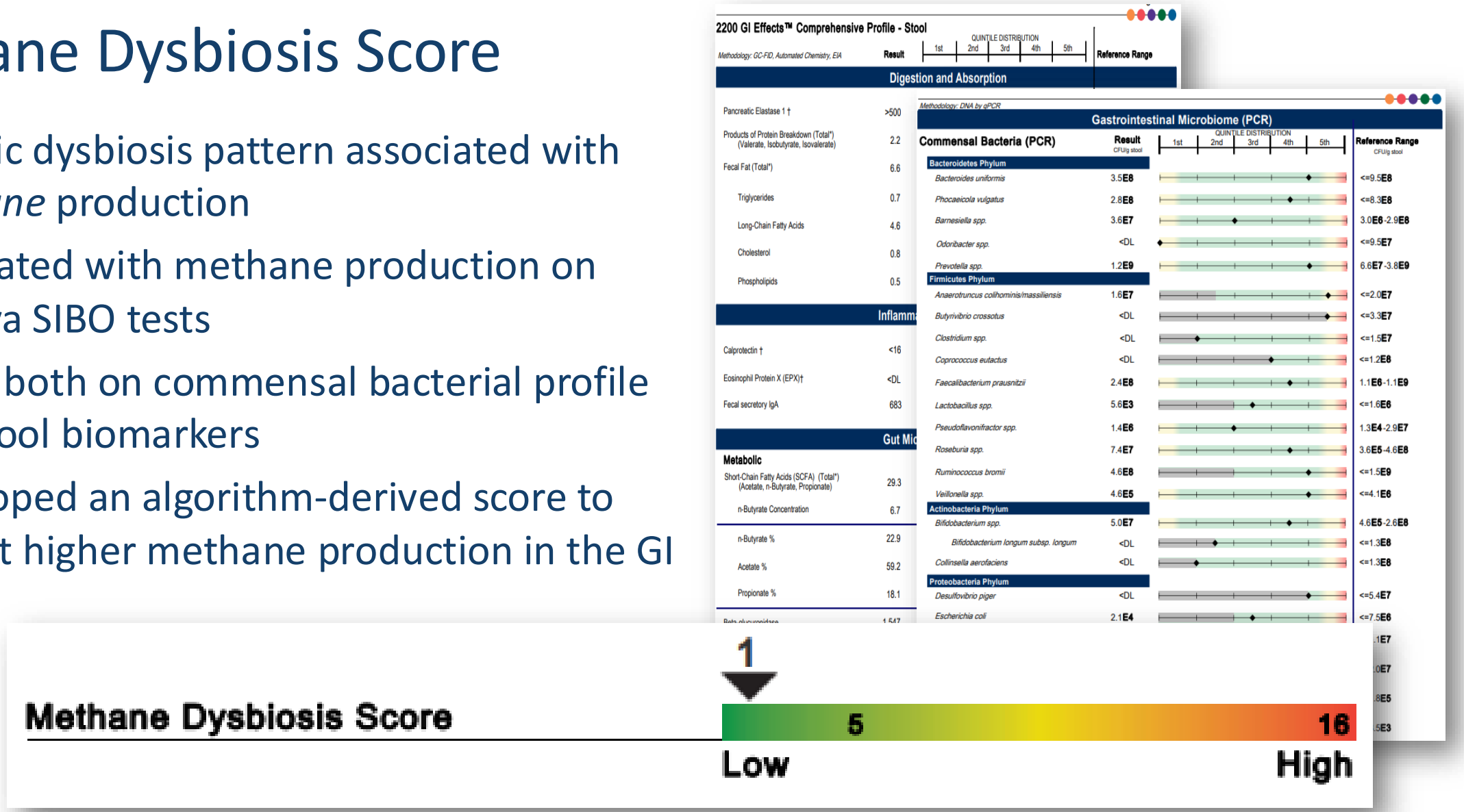
- Specific dysbiosis pattern associated with inflammation
- Correlated with inflammatory biomarkers
  - Calprotectin
  - Eosinophil Protein X
  - Secretory IgA
- Algorithm-derived from commensal bacteria analysis



GENOVA DIAGNOSTICS

Methane Dysbiosis Score

- Specific dysbiosis pattern associated with *methane* production
- Correlated with methane production on Genova SIBO tests
- Based both on commensal bacterial profile and stool biomarkers
- Developed an algorithm-derived score to predict higher methane production in the GI tract



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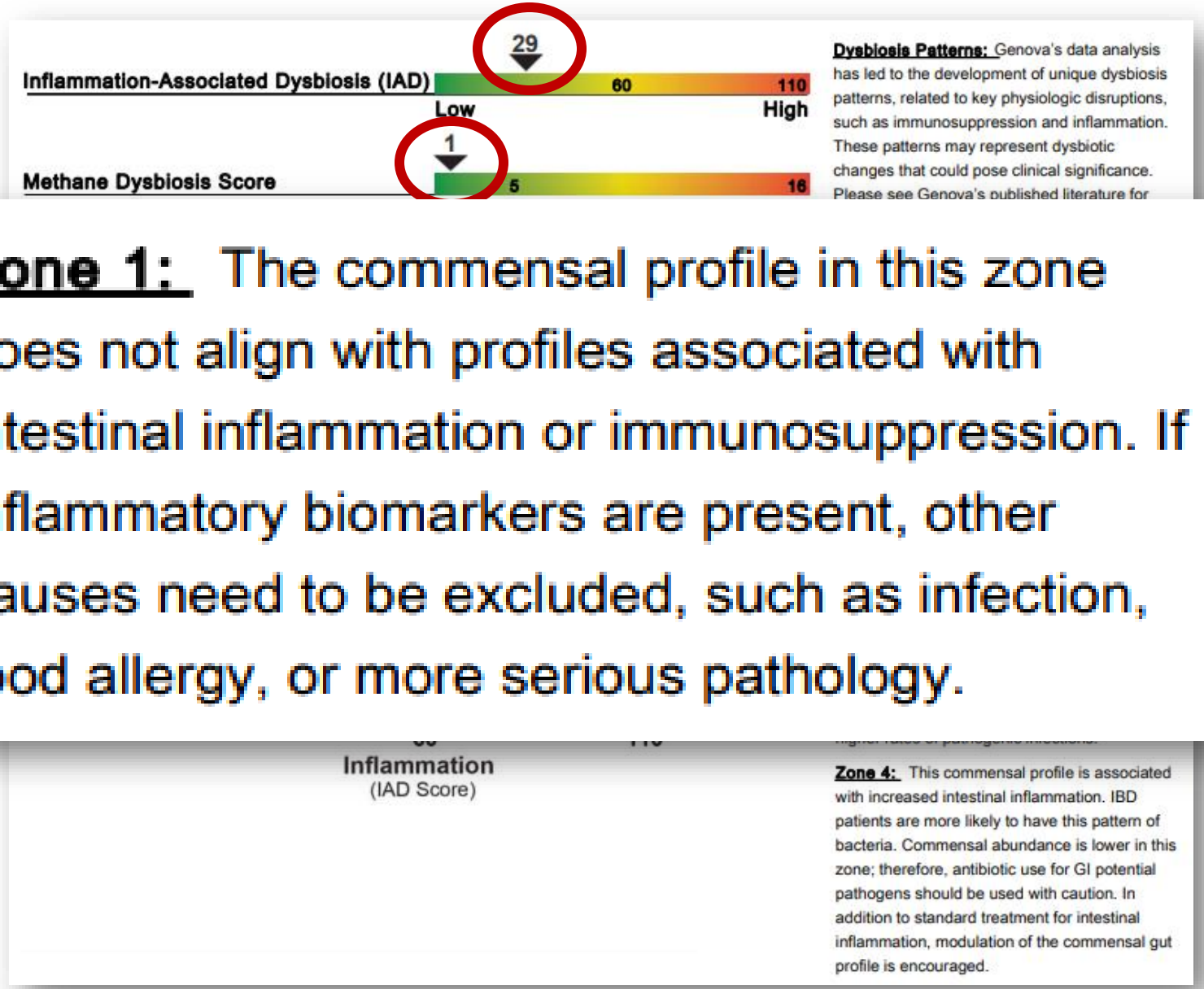
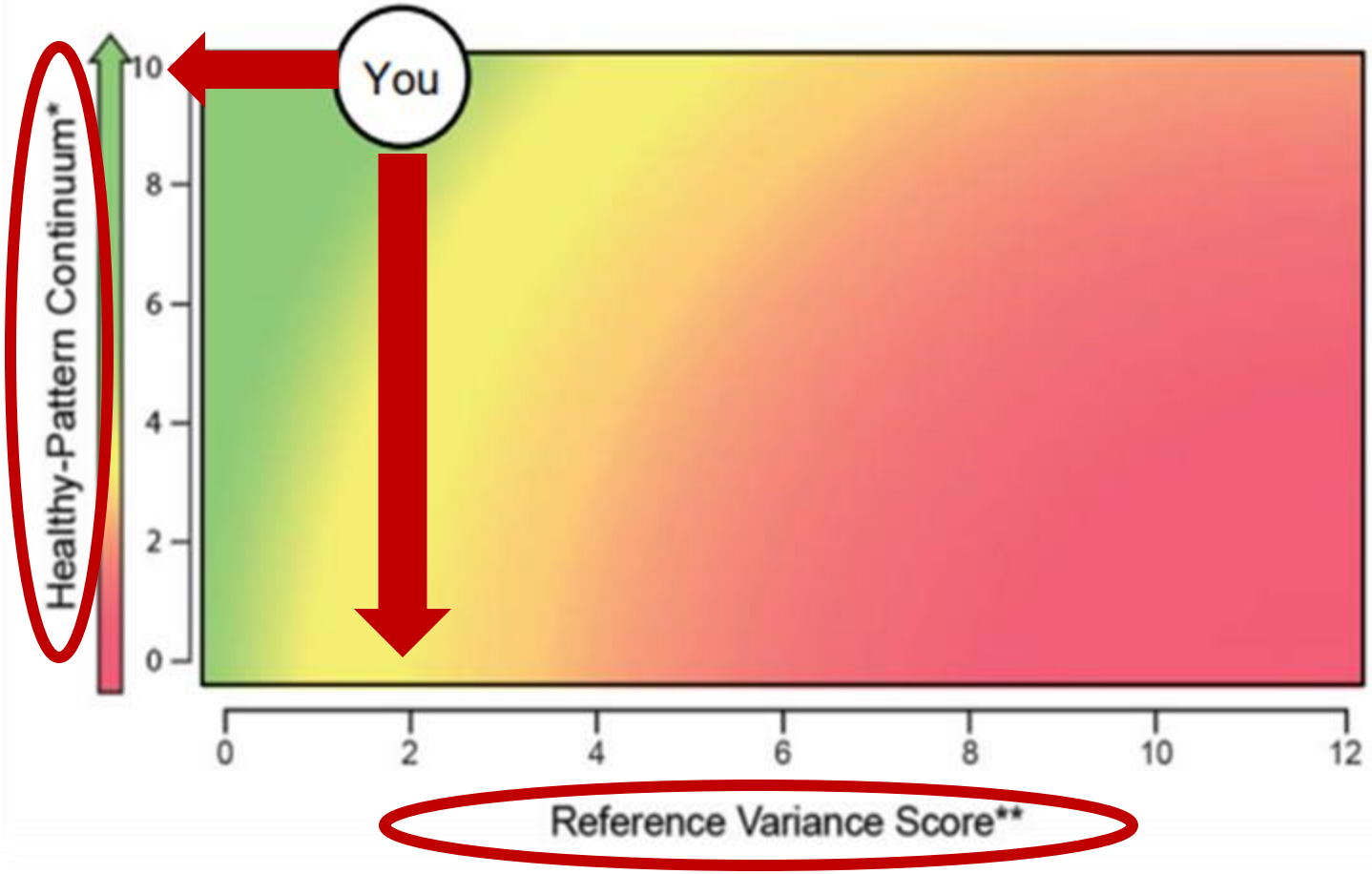
Dysbiosis Patterns



GENOVA DIAGNOSTICS

Commensal Microbiome Analysis

Commensal Balance



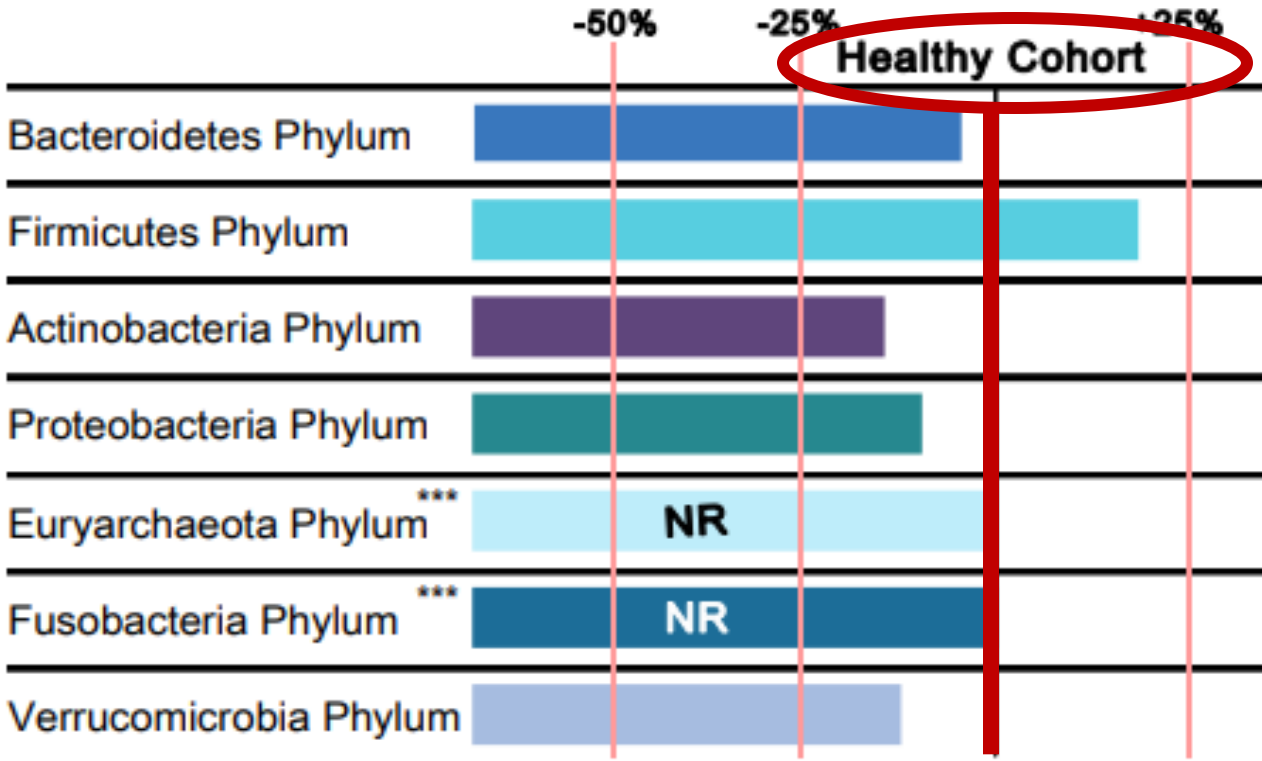
Balanced	Represents 95% of healthy individuals
Borderline	Represents 5% of healthy individuals
Imbalanced	Represents 60% of unhealthy individuals

*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

**The total number of commensal bacteria (qPCR) that are out of balance for this individual on a scale of 0 to >12.

GENOVA DIAGNOSTICS®

Relative Commensal Abundance



Increase in *Bacteroides* spp. and *Odoribacter* spp. seen in animal-based diets; *Prevotella* increased with plant-based diet

Contains many butyrate-producers; most species responsive to plant-based diets; *Faecalibacterium* spp. is anti-inflammatory

Bifidobacterium is increased with plant-based diets; *Collinsella* may be proinflammatory, and is elevated with a Western-diet

Some species may be proinflammatory; *E. coli* consumes simple sugars and is lower in individuals on plant-based diets

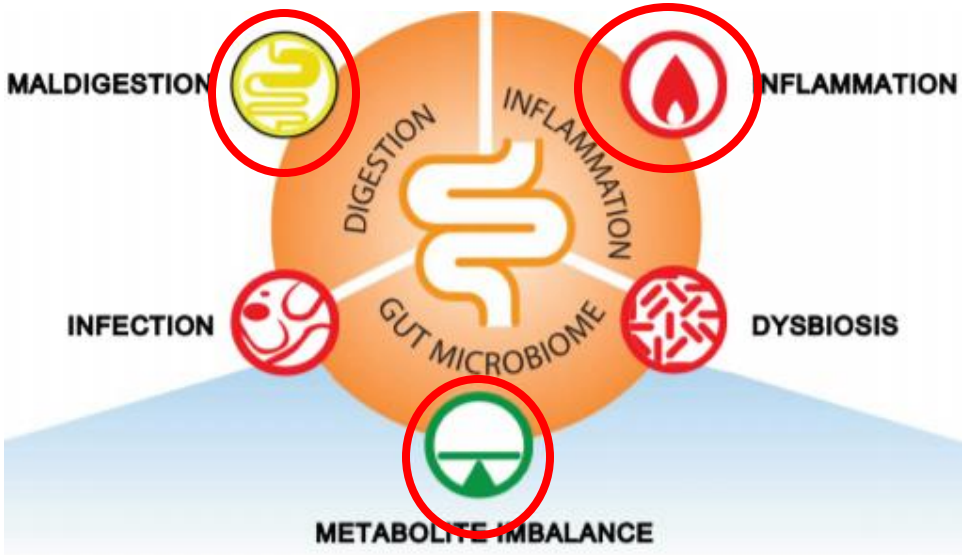
Methanobrevibacter smithii is associated with methane production and with diets high in carbohydrates

Certain *Fusobacterium* spp. may be proinflammatory and increased on low fiber, high fat diets

Akkermansia spp. is involved in gut membrane integrity and may be increased with polyphenols and prebiotics

Relative Abundance: The relative abundance compares the quantity of each of 7 major bacterial phyla to a healthy cohort. This can indicate broader variances in the patient's gut microbiome profile. Certain interventions may promote or limit individual phyla when clinically appropriate. Please refer to Genova's Stool Testing Support Guide for more information on modulation of commensal bacteria through diet & nutrient interventions. ***Approximately 70% of the healthy cohort had below detectable levels of *Methanobrevibacter smithii*. Approximately 90% of the healthy cohort had below detectable levels of *Fusobacterium spp.*

GENOVA DIAGNOSTICS



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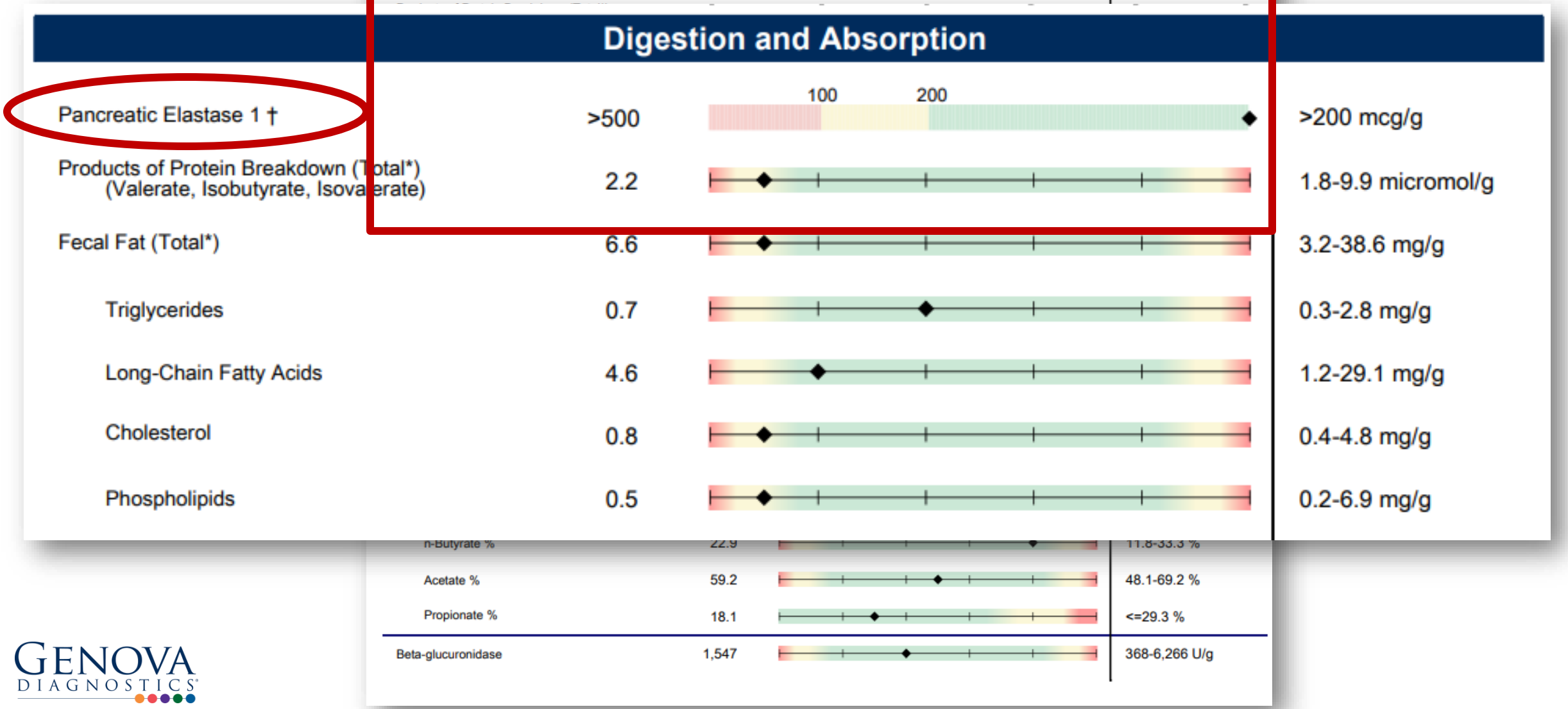
2200 GI Effects™ Comprehensive Profile - Stool

Methodology: GC/MS, Automated Chemistry, EIA

	Result	QUINTILE DISTRIBUTION (1st 2nd 3rd 4th 5th)	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	158 L	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	6.0		1.8-9.9 micromol/g
Fecal Fat (Total*)	19.5		3.2-38.6 mg/g
Triglycerides	1.1		0.3-2.8 mg/g
Long-Chain Fatty Acids	12.9		1.2-29.1 mg/g
Cholesterol	0.5		0.4-4.8 mg/g
Phospholipids	5.0		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	145 H		<=50 mcg/g
Eosinophil Protein X (EPX)†	4.9 H	1.1 4.6	<=4.6 mcg/g
Fecal secretory IgA	206		<=885 mcg/g
Gastrointestinal Microbiome			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	81.3		>=23.3 micromol/g
n-Butyrate Concentration	18.1		>=3.6 micromol/g
n-Butyrate %	22.3		11.8-33.3 %
Acetate %	63.1		48.1-69.2 %
Propionate %	14.6		<=29.3 %
Beta-glucuronidase	2,297		368-6,266 U/g

GENOVA DIAGNOSTICS

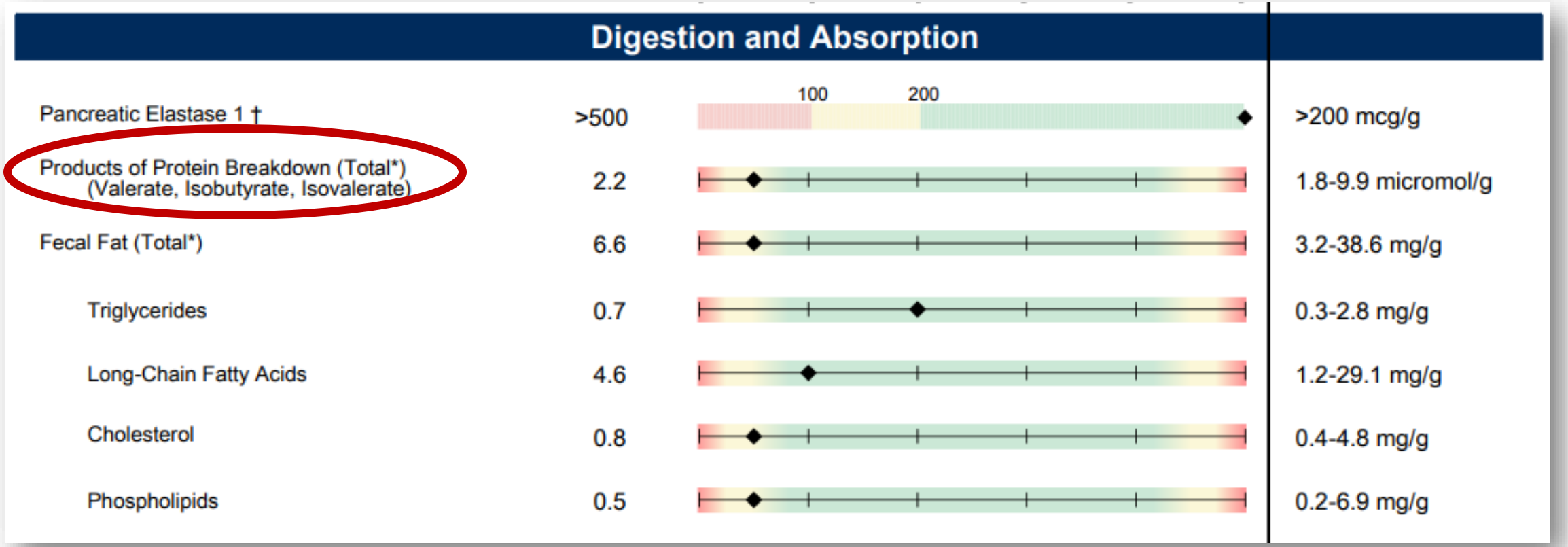


GENOVA DIAGNOSTICS

Pancreatic Elastase 1

- A digestive enzyme secreted by the pancreas providing insight into pancreatic exocrine function
- Not affected by transit time, though profuse watery stool samples may falsely lower PE-1 due to dilution
- Not affected by digestive enzyme supplementation
- PE-1 correlates with the gold-standard secretin-cerulean test
- Low levels associated with chronic pancreatitis, gallstones, gastric bypass, Celiac disease, Diabetes, IBD, obesity

Products of Protein Breakdown

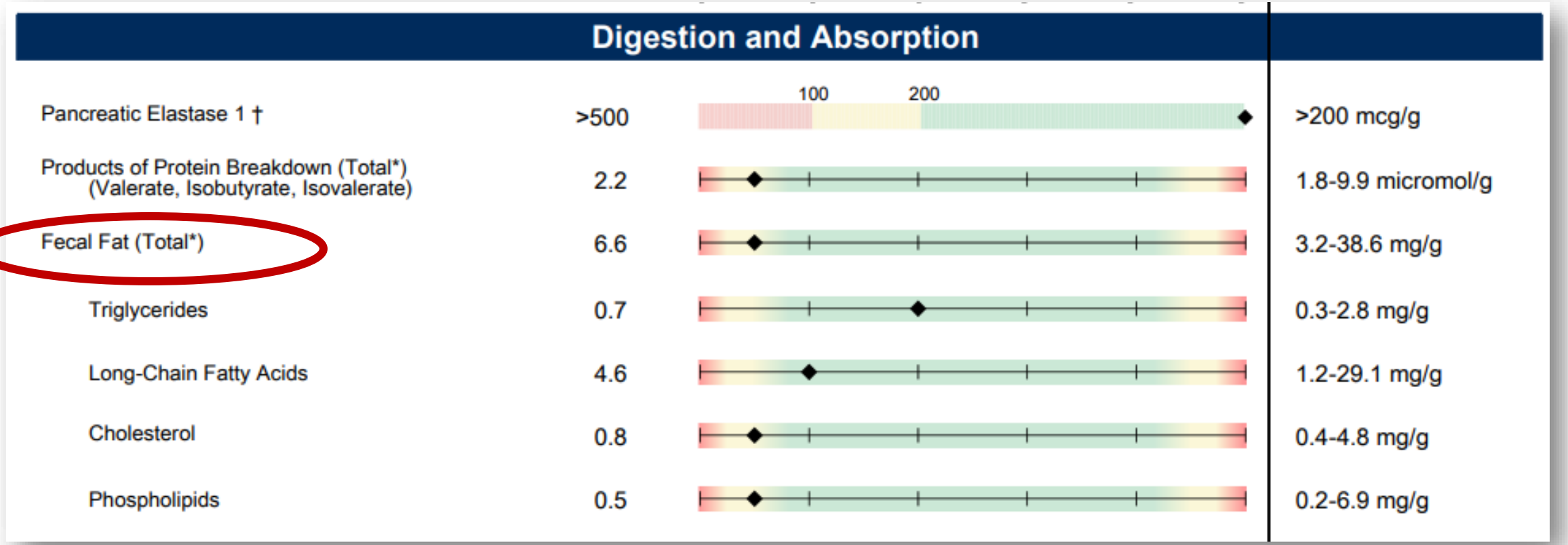


GENOVA DIAGNOSTICS

Products of Protein Breakdown

- Dietary protein not digested or absorbed effectively by the small intestine may be exposed to anaerobes in the colon which ferment them into **Products of Protein Breakdown**
- Elevations may reflect poor digestion/absorption of protein
- Dietary intake can influence elevated findings based on higher protein volume
- Conversely, lower levels may indicate effective digestion/absorption of protein and/or lower dietary intake
- May reflect hypochlorhydria
- Check for SIBO
- Check for inflammation or infection

Fecal Fats



GENOVA DIAGNOSTICS

Fecal Fats

- Your patients should include fats as an essential component of their diets, elevated fecal fats imply poor digestion/absorption of those fats
- Triglycerides and cholesterol make up most of our dietary fat intake
- Triglycerides are broken down to form LCFAs
- Elevated fecal fats can be caused by:
  - Exocrine pancreatic insufficiency
  - Bile salt insufficiency
  - Use of PPIs and hypochlorhydria

Digestion and Absorption

Pancreatic Elastase 1 †	>500	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	2.2		1.8-9.9 micromol/g
Fecal Fat (Total*)	6.6		3.2-38.6 mg/g
Triglycerides	0.7		0.3-2.8 mg/g
Long-Chain Fatty Acids	4.6		1.2-29.1 mg/g
Cholesterol	0.8		0.4-4.8 mg/g
Phospholipids	0.5		0.2-6.9 mg/g

Inflammation and Immunology

Calprotectin †	<16	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	<DL	0.5 2.7	<=2.7 mcg/g
Fecal secretory IgA	683	680 2040	<=2,040 mcg/mL

Gut Microbiome Metabolites

Metabolic

Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	29.3		>=23.3 micromol/g
n-Butyrate Concentration	6.7		>=3.6 micromol/g
n-Butyrate %	22.9		11.8-33.3 %
Acetate %	59.2		48.1-69.2 %
Propionate %	18.1		<=29.3 %
Beta-glucuronidase	1,547		368-6,266 U/g

GENOVA DIAGNOSTICS

Calprotectin

- Released from the intestinal mucosa into the stool in intestinal inflammation
- Fecal calprotectin is useful in differentiating IBD from IBS and monitoring IBD treatment
- It is ***not*** a cancer marker
- It is not a substitute for a scope, but can certainly direct the physician to the usefulness of scoping the patient
- Calprotectin 50-120 mcg/g can be caused by infection, hx of IBD, chronic NSAID or PPI use
- Calprotectin >120 refer to GI specialist to rule out IBD, malignancy

Eosinophil Protein X (EPX)

Inflammation and Immunology			
Calprotectin †	<16	50 / 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	<DL	0.5 / 2.7	<=2.7 mcg/g
Fecal secretory IgA	683	680 / 2040	<=2,040 mcg/mL

GENOVA DIAGNOSTICS

Eosinophil Protein X (EPX)

- Elevated with immune-mediated food hypersensitivity, atopic dermatitis and food allergies
- Inflammatory Bowel Disease (IBD)
- Certain parasitic infections
- Microscopic colitis (dx requires histological analysis)
- Can be elevated in children younger than 4 years old

Fecal Secretory IgA

Inflammation and Immunology			
Calprotectin †	<16	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	<DL	0.5 2.7	<=2.7 mcg/g
Fecal secretory IgA	683	680 2040	<=2,040 mcg/mL

GENOVA DIAGNOSTICS

Fecal Secretory IgA

- Recognized as a first line of defense in protecting the intestinal epithelium from enteric pathogens
- Examples include Celiac disease, colon cancer, infections, IBS
- Treat root causes of immune upregulation/inflammation
- Assess for intestinal permeability
- Assess food antibody testing, consider use of an elimination diet
- Low sIgA may reflect a loss of GI immune response resiliency

Digestion and Absorption

Pancreatic Elastase 1 †	>500	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	2.2		1.8-9.9 micromol/g
Fecal Fat (Total*)	6.6		3.2-38.6 mg/g
Triglycerides	0.7		0.3-2.8 mg/g
Long-Chain Fatty Acids	4.6		1.2-29.1 mg/g
Cholesterol	0.8		0.4-4.8 mg/g
Phospholipids	0.5		0.2-6.9 mg/g

Inflammation and Immunology

Calprotectin †	<16	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	<DL	0.5 2.7	<=2.7 mcg/g
Fecal secretory IgA	683	680 2040	<=2,040 mcg/mL

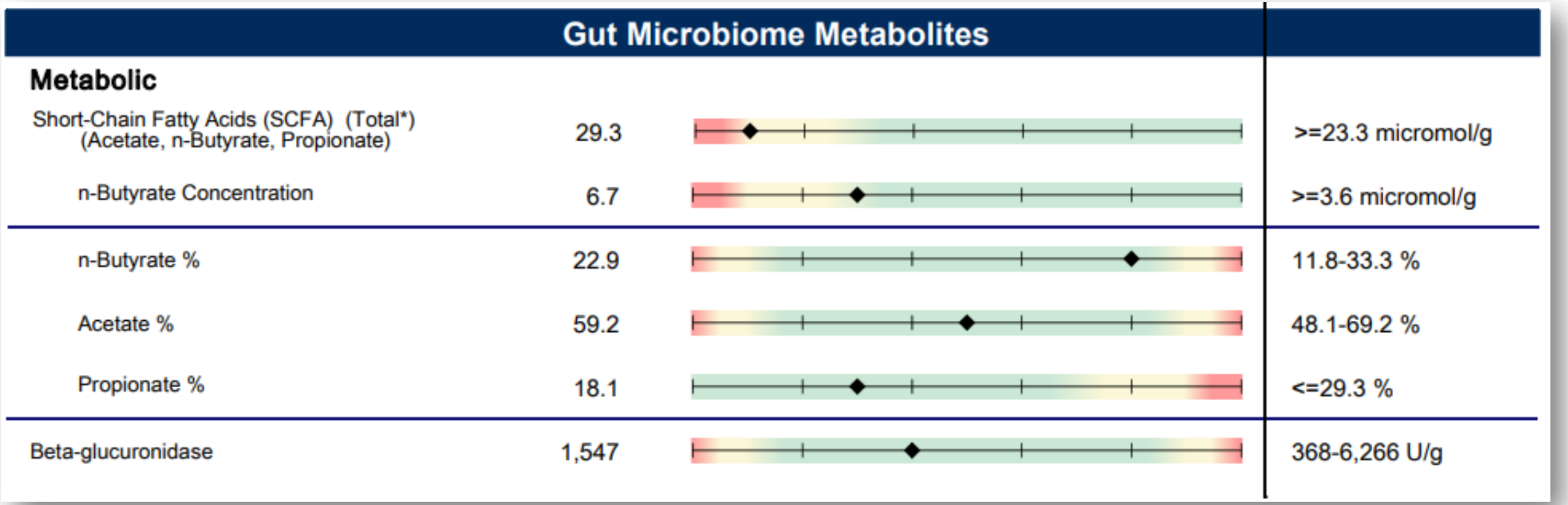
Gut Microbiome Metabolites

Metabolic

Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	29.3		>=23.3 micromol/g
n-Butyrate Concentration	6.7		>=3.6 micromol/g
n-Butyrate %	22.9		11.8-33.3 %
Acetate %	59.2		48.1-69.2 %
Propionate %	18.1		<=29.3 %
Beta-glucuronidase	1,547		368-6,266 U/g

GENOVA DIAGNOSTICS

Short-Chain Fatty Acids



Gut Microbiome Metabolites			
Metabolic			
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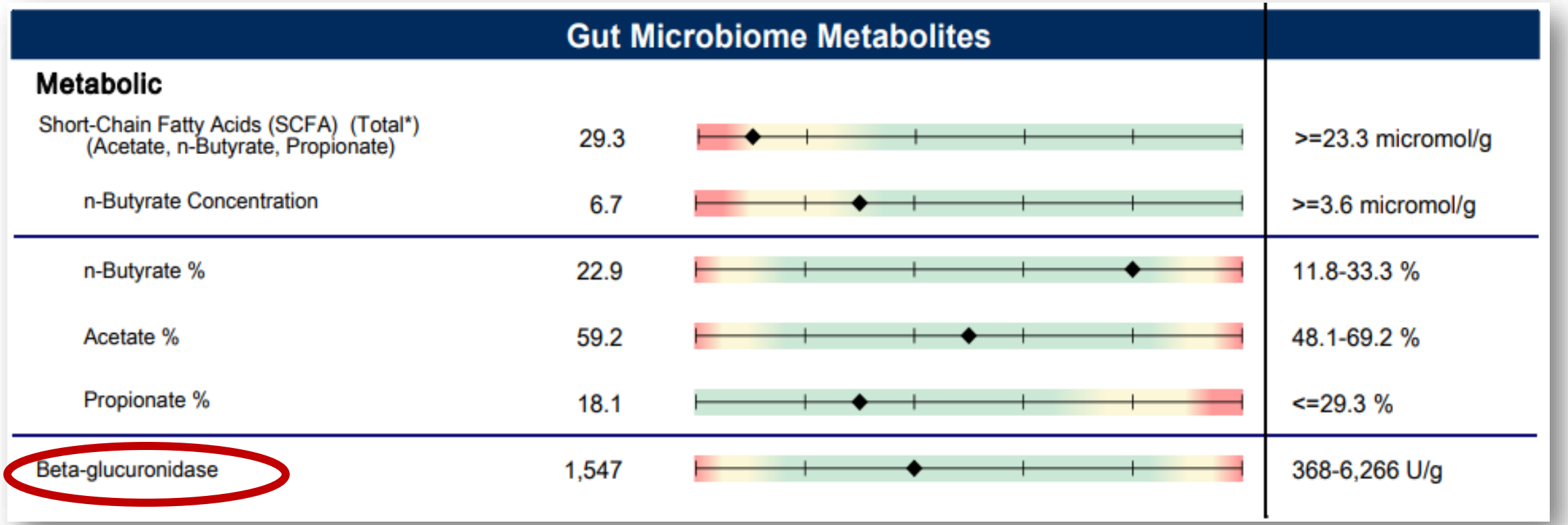
n-Butyrate %	22.9		11.8-33.3 %
Acetate %	59.2		48.1-69.2 %
Propionate %	18.1		<=29.3 %
Beta-glucuronidase	1,547		368-6,266 U/g

GENOVA DIAGNOSTICS

Short-Chain Fatty Acids

- Acetate, proprionate and butyrate are produced by bacterial fermentation of dietary fiber and resistant starch
- They act to maintain intestinal barrier function
- Provide fuel for colonocytes
- Support commensal bacteria
- Modulated anti-inflammatory and antimicrobial activities

Beta-glucuronidase



Gut Microbiome Metabolites			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	29.3		>=23.3 micromol/g
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Acetate %	59.2		48.1-69.2 %
Propionate %	18.1		<=29.3 %
Beta-glucuronidase	1,547		368-6,266 U/g

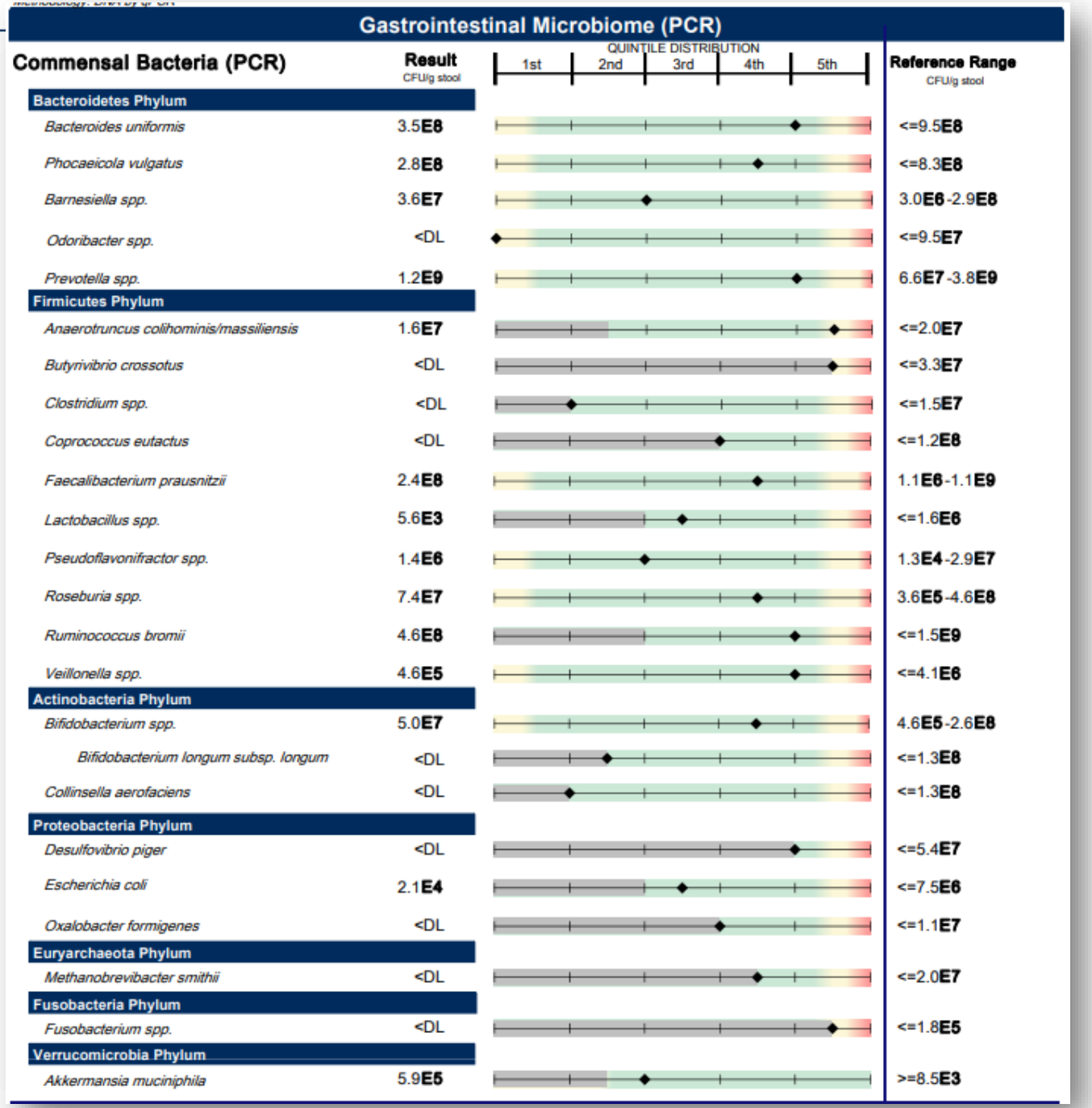
GENOVA DIAGNOSTICS

Beta-glucuronidase

- An enzyme produced by colonocytes and intestinal bacteria
- Can promote recirculation of various hormones and toxins that would have been eliminated
- Its action can therefore increase circulating estrogens
- Research suggests an association with increased risk of colorectal and breast cancer
- Elevation caused by dysbiosis and a Western diet high in red meat and protein
- Therapeutic considerations include probiotics, dietary fiber, Calcium-D-glucarate (found in oranges, apples, grapefruit and cruciferous vegetables)
- Low-calorie and vegetarian diets
- Konjac noodles are known to inhibit the action of the enzyme

Commensal Bacteria (PCR)

- Commensals are not inherently pathogenic
- Pattern analysis allows for better interpretation of findings
- PCR is quantitative
- Individual bacteria have unique clinical associations and importance to GI health
- PDF lists each individually with information on each



Gastrointestinal Microbiome (PCR)

Commensal Bacteria (PCR)	Result (CFU/g stool)	Reference Range (CFU/g stool)
Bacteroidetes Phylum		
Bacteroides uniformis	3.5E8	<=9.5E8
Phocaeicola vulgatus	2.8E8	<=8.3E8
Barnesiella spp.	3.6E7	3.0E6-2.9E8
Odoribacter spp.	<DL	<=9.5E7
Prevotella spp.	1.2E9	6.6E7-3.8E9
Firmicutes Phylum		
Anaerotruncus colihominis/massiliensis	1.6E7	<=2.0E7
Butyrivibrio crossotus	<DL	<=3.3E7
Clostridium spp.	<DL	<=1.5E7
Coprococcus eutactus	<DL	<=1.2E8
Faecalibacterium prausnitzii	2.4E8	1.1E6-1.1E9
Lactobacillus spp.	5.6E3	<=1.6E6
Pseudoflavonifractor spp.	1.4E6	1.3E4-2.9E7
Roseburia spp.	7.4E7	3.6E5-4.6E8
Ruminococcus bromii	4.6E8	<=1.5E9
Veillonella spp.	4.6E5	<=4.1E6
Actinobacteria Phylum		
Bifidobacterium spp.	5.0E7	4.6E5-2.6E8
Bifidobacterium longum subsp. longum	<DL	<=1.3E8
Collinsella aerofaciens	<DL	<=1.3E8
Proteobacteria Phylum		
Desulfovibrio piger	<DL	<=5.4E7
Escherichia coli	2.1E4	<=7.5E6
Oxalobacter formigenes	<DL	<=1.1E7
Euryarchaeota Phylum		
Methanobrevibacter smithii	<DL	<=2.0E7
Fusobacteria Phylum		
Fusobacterium spp.	<DL	<=1.8E5
Verrucomicrobia Phylum		
Akkermansia muciniphila	5.9E5	>=8.5E3

QUINTILE DISTRIBUTION: 1st | 2nd | 3rd | 4th | 5th

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Commensal Bacteria Guide

Commensal Bacteria

The most current, literature-based information on human studies related to increased or decreased levels of the commensal bacteria is summarized in the following chart. Note that the findings in the literature may not be consistent with Genova's findings due to different methodologies, thus treatment efficacy may vary. Most therapeutic interventions do not work in isolation, meaning they do not exclusively only target that one organism. Genova has not conducted outcome studies on the impact of certain therapeutics on the microbiome markers. Clinician discretion is advised for appropriateness of therapeutics.

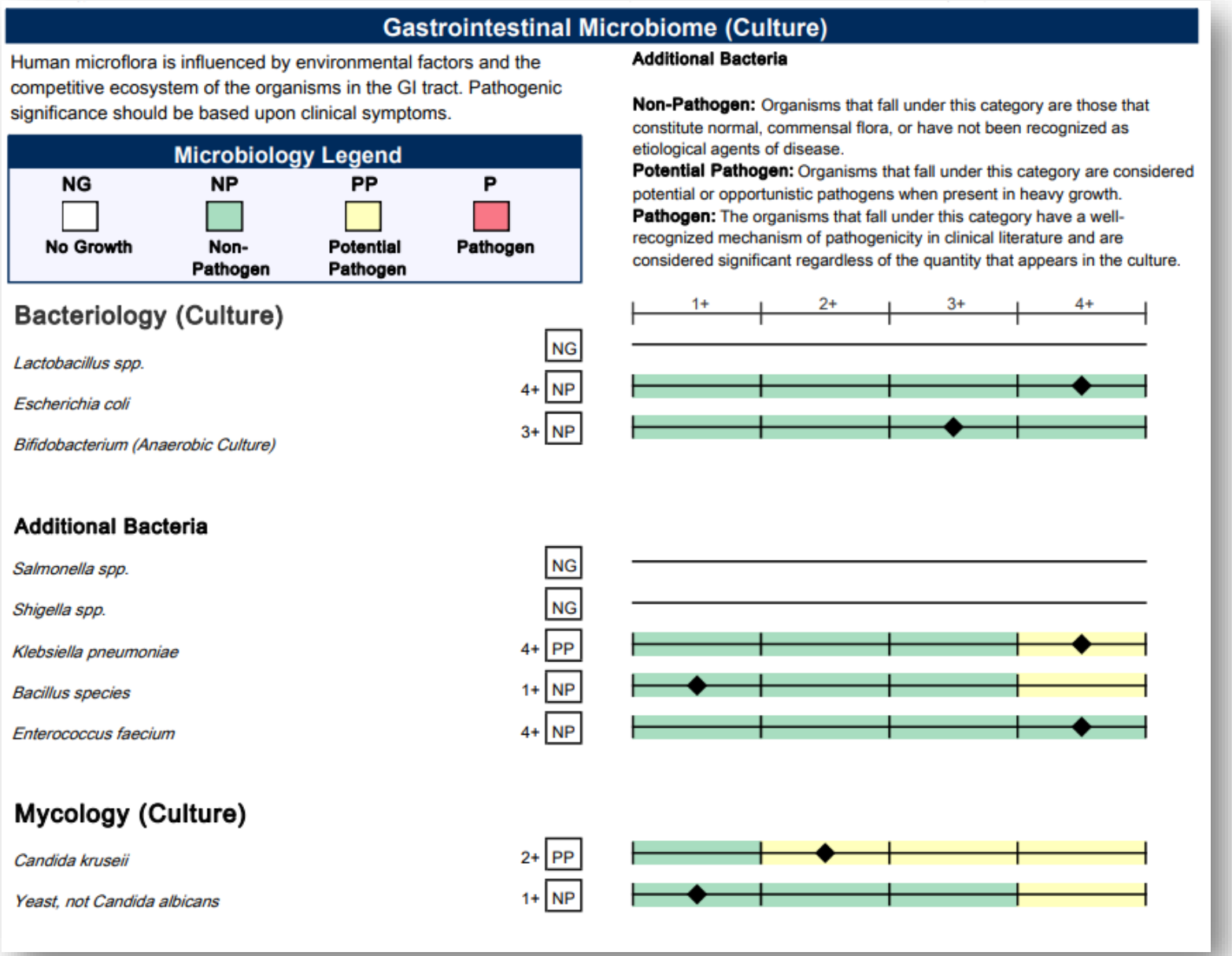
Under certain conditions, environmental factors may influence specific commensals to become pathobionts. Pathobionts are distinguished from true infectious agents; they are potential pathogens under certain conditions. It is unknown whether these organisms play a causative role in disease or are a consequence of a disease state. Literature is evolving regarding the definition of a pathobiont and the role of commensal bacteria.[1-3]

Organism	Description	Increased Levels	Decreased Levels
Bacteroides uniformis	*Bacteroides uniformis* is a fiber-degrading bacteria. It colonizes the gut in early infancy and is promoted by breast feeding.[4] Thought to enhance the gut barrier through the production of butyrate and GABA.[5,6] Also produces beta glucuronidase, degrades mucin, and produces folate.[4,7,8] Studied in preclinical trials as a potential probiotic for use in inflammatory and metabolic disorders.[9-11] *B. uniformis* was found to be decreased in obese patients as compared to healthy or lean groups.[12,13] It was higher in healthy controls as compared to patients with ulcerative colitis.[14] Enriched in healthy individuals versus colorectal cancer patients.[15] Associated with degradation of the isoflavone genistein, which then becomes less bioavailable to the human.[16]	In ten healthy males, the consumption of red wine polyphenols for 4 weeks significantly increased the amount of *Bacteroides uniformis* as well as other commensal bacteria species.[17] Higher levels of insoluble fiber are associated with higher levels of *B. uniformis*.[18] A more favorable metabolic risk profile in men on a healthy plant-based diet was seen with a certain microbial profile featuring increased *B. uniformis* and decreased *Prevotella copri*. The healthy diet was characterized by a higher intake of fiber, plant proteins, whole grains, fruits, vegetables, nuts, and legumes, and a lower intake of energy, animal proteins, refined grains, potatoes, sweets, animal fat, egg, dairy, and meats.[19] A small study (n=13) showed the presence of *B. uniformis* and other *Bacteroides* species in non-vegetarians, versus vegetarians.[20]	Higher fiber intake from beans is associated with lower abundance of *B. uniformis*.[21]
Phocaeicola vulgatus	Generally considered a beneficial gut commensal, although is capable of attaching to and invading colonic epithelial cells and inducing pro-inflammatory cytokines.[22] Produces beta-glucuronidase, succinate, lactate, acetate, formate, and propionate.[23,24]	A high beef diet was associated with increases in *Bacteroides fragilis, B. vulgatus* and *Clostridium* spp. in 10 volunteers.[27]	Decreased levels were found in 7-12-year olds who consumed oligofructose-enriched inulin (*BENEO's* prebiotic fiber *Synergy1*) for 16 weeks in a double-blind-controlled trial.[28]

GENOVA DIAGNOSTICS®

Stool Culture

- Culture means it is living, which means sensitivities can be used for treatment protocol design
- Genova distinguishes pathogens, potential pathogens and non-pathogen findings
- Mycology is culture specific to viable yeast growth



Gastrointestinal Microbiome (Culture)

Human microflora is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathogenic significance should be based upon clinical symptoms.

Microbiology Legend

NG	NP	PP	P
No Growth	Non-Pathogen	Potential Pathogen	Pathogen

Additional Bacteria

Non-Pathogen: Organisms that fall under this category are those that constitute normal, commensal flora, or have not been recognized as etiological agents of disease.
Potential Pathogen: Organisms that fall under this category are considered potential or opportunistic pathogens when present in heavy growth.
Pathogen: The organisms that fall under this category have a well-recognized mechanism of pathogenicity in clinical literature and are considered significant regardless of the quantity that appears in the culture.

Bacteriology (Culture)

		1+ 2+ 3+ 4+
Lactobacillus spp.	NG	
Escherichia coli	4+ NP	
Bifidobacterium (Anaerobic Culture)	3+ NP	

Additional Bacteria

Salmonella spp.	NG	
Shigella spp.	NG	
Klebsiella pneumoniae	4+ PP	
Bacillus species	1+ NP	
Enterococcus faecium	4+ NP	

Mycology (Culture)

Candida kruseii	2+ PP	
Yeast, not Candida albicans	1+ NP	

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Gastrointestinal Microbiome (Culture)

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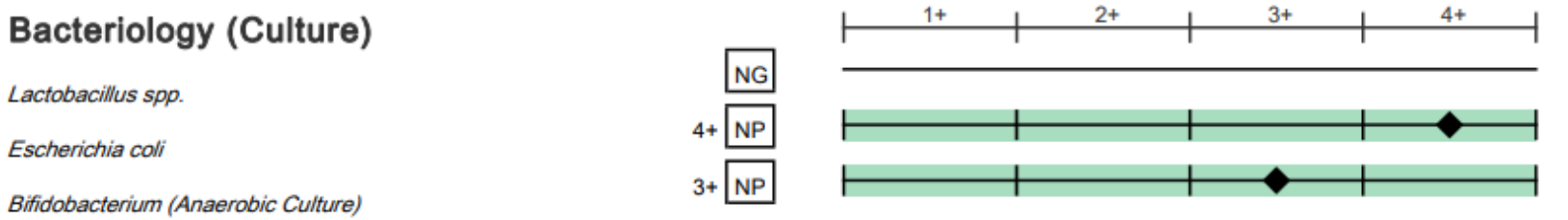
Bacteriology (Culture)

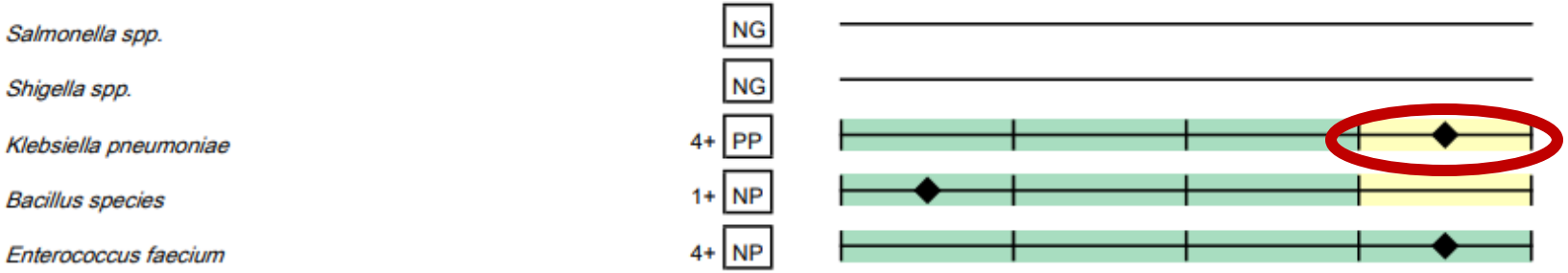


Lactobacillus spp.

Escherichia coli

Bifidobacterium (Anaerobic Culture)

Additional Bacteria



Salmonella spp.

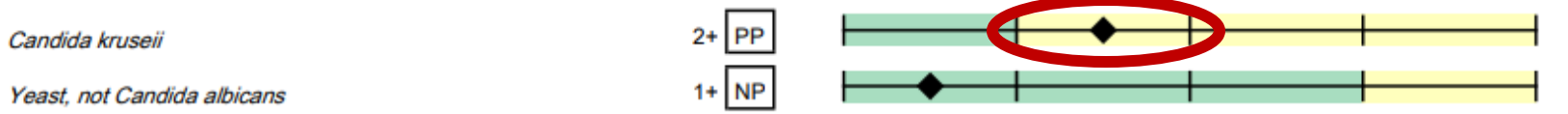
Shigella spp.

Klebsiella pneumoniae

Bacillus species

Enterococcus faecium

Mycology (Culture)



Candida kruseii

Yeast, not Candida albicans

GENOVA DIAGNOSTICS

Methodology: Vitek 2® System Microbial Antibiotic susceptibility, Manual Minimum Inhibition Concentration

Bacteria Sensitivity

Prescriptive Agents

Klebsiella pneumoniae	R	I	S-DD	S	NI
Ampicillin	R				
Amox./Clavulanic Acid				S	
Cephalothin				S	
Ciprofloxacin				S	
Tetracycline				S	
Trimethoprim/Sulfa				S	

Natural Agents

Klebsiella pneumoniae	LOW INHIBITION	HIGH INHIBITION
Berberine		
Oregano		
Uva-Ursi		

GENOVA DIAGNOSTICS®

Methodology: Vitek 2® System Microbial Antibiotic susceptibility, Manual Minimum Inhibition Concentration

Mycology Sensitivity

Candida Susceptibility Profile for Azoles*

Organism	Number of Isolates	% Sensitive	
		Fluconazole	Voriconazole
Candida albicans	25561	99.19%	99.51%
Candida parapsilosis	8777	98.64%	99.33%
Candida kruseii	3420	0.23%	97.79%
Candida tropicalis	1076	93.22%	90.57%
Candida glabrata	2898	27.1%	90.9%

Results of pharmaceutical sensitivities against certain yeast species are based on internal Genova data pertaining to the frequency of susceptibility of the specific yeast to the listed antifungal agent. The pharmaceutical results are not patient-specific. Conversely, the results of inhibition to nystatin and natural agents are patient-specific.

Non-absorbed Antifungals

Candida kruseii	LOW INHIBITION	HIGH INHIBITION
Nystatin		

Natural Agents

Candida kruseii	LOW INHIBITION	HIGH INHIBITION
Berberine		
Caprylic Acid		
Garlic		
Undecylenic Acid		
Uva-Ursi		

GENOVA DIAGNOSTICS®

Microscopic O&P Parasite

- Choice of one specimen or 3 over different days to cast a wider net
- Microscopic exam allows for a much wider capacity to identify parasites
- Includes WBC and Charcot-Leyden Crystals
- Findings of Few, Moderate, Many

Parasitology

Microscopic O&P Results

Microscopic O&P is capable of detecting all described gastrointestinal parasites. The organisms listed in the box represent those commonly found in microscopic stool analysis. Should an organism be detected that is not included in the list below, it will be reported in the Additional Results section. These results were obtained using wet preparation(s) and trichrome stained smear. For an extensive reference of all potentially detectable organisms, please visit www.gdx.net/product/gi-effects-comprehensive-stool-test

Genus/species	Result
Nematodes - roundworms	
Ancylostoma/Necator (Hookworm)	Not Detected
Ascaris lumbricoides	Not Detected
Capillaria philippinensis	Not Detected
Enterobius vermicularis	Not Detected
Strongyloides stercoralis	Not Detected
Trichuris trichiura	Not Detected
Cestodes - tapeworms	
Diphyllobothrium latum	Not Detected
Dipylidium caninum	Not Detected
Hymenolepis diminuta	Not Detected
Hymenolepis nana	Not Detected
Taenia spp.	Not Detected
Trematodes - flukes	
Clonorchis/Opisthorchis spp.	Not Detected
Fasciola spp./ *Fasciolopsis buski*	Not Detected
Heterophyes/Metagonimus	Not Detected
Paragonimus spp.	Not Detected
Schistosoma spp.	Not Detected
Protozoa	
Balantidium coli	Not Detected
Blastocystis spp.	**Many Detected**
Chilomastix mesnili	Not Detected
Cryptosporidium spp.	Not Detected
Cyclospora cayetanensis	Not Detected
Dientamoeba fragilis	Not Detected
Entamoeba coli	Not Detected
Entamoeba histolytica/dispar	Not Detected
Entamoeba hartmanii	Not Detected
Entamoeba polecki	Not Detected
Endolimax nana	Not Detected
Giardia	Not Detected
Iodamoeba buetschlii	Not Detected
Cystoisospora spp.	Not Detected
Trichomonads (e.g. *Pentatrichomonas*)	Not Detected
Additional Findings	
White Blood Cells	Not Detected
Charcot-Leyden Crystals	Not Detected
Other Infectious Findings	

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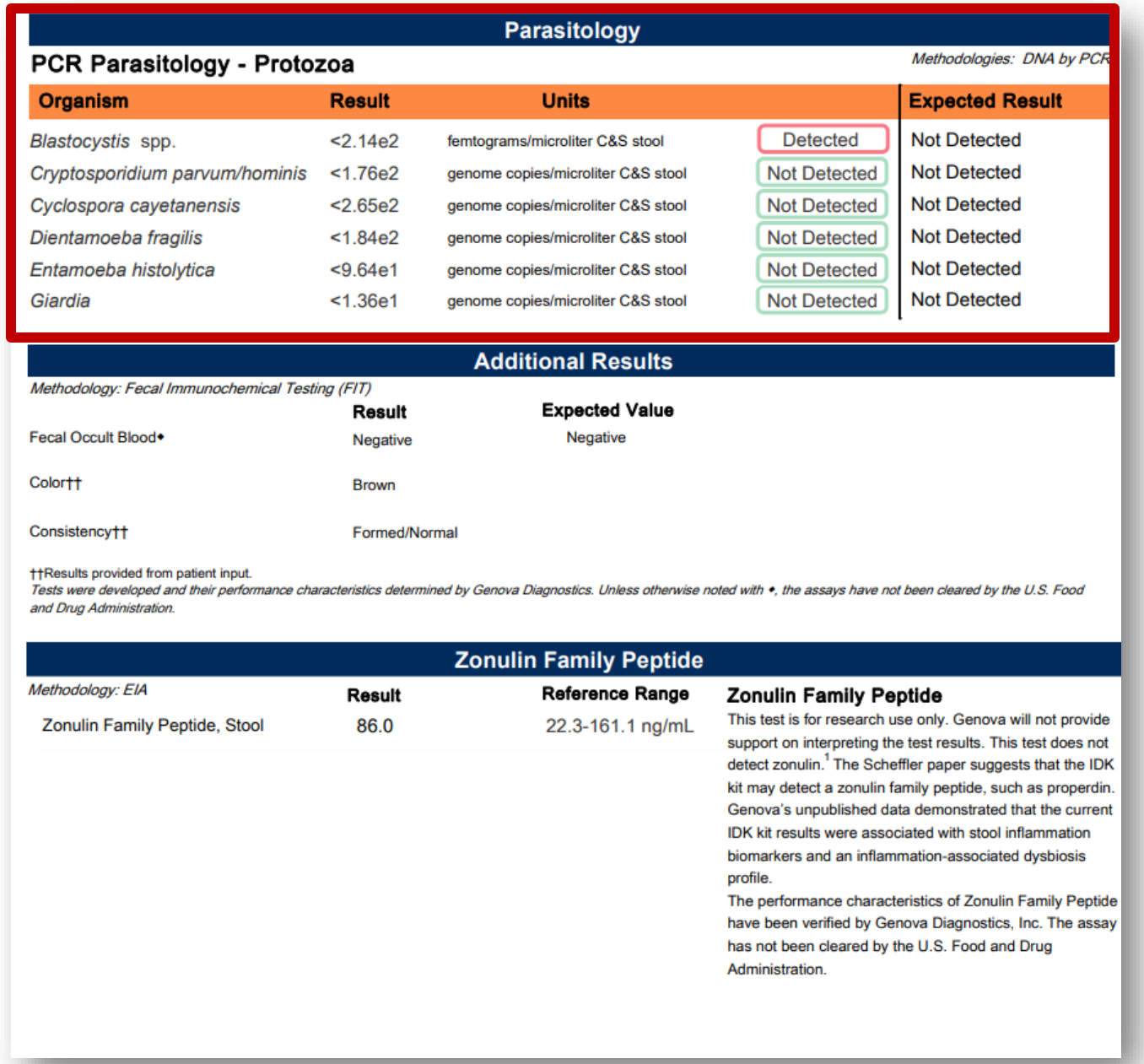
PCR Parasitology

- PCR detection can only find those parasites the test is designed specifically to identify
- Combining PCR with Microscopic O&P provides a much wider possibility for detection
- Why don't we provide sensitivities for parasites?



Parasitology

PCR Parasitology - Protozoa

Methodologies: DNA by PCR

Organism	Result	Units		Expected Result
Blastocystis spp.	<2.14e2	femtograms/microliter C&S stool	Detected	Not Detected
Cryptosporidium parvum/hominis	<1.76e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Cyclospora cayetanensis	<2.65e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Dientamoeba fragilis	<1.84e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Entamoeba histolytica	<9.64e1	genome copies/microliter C&S stool	Not Detected	Not Detected
Giardia	<1.36e1	genome copies/microliter C&S stool	Not Detected	Not Detected

Additional Results

Methodology: Fecal Immunochemical Testing (FIT)

	Result	Expected Value
Fecal Occult Blood♦	Negative	Negative
Color††	Brown	
Consistency††	Formed/Normal	

††Results provided from patient input.
Tests were developed and their performance characteristics determined by Genova Diagnostics. Unless otherwise noted with ♦, the assays have not been cleared by the U.S. Food and Drug Administration.

Zonulin Family Peptide

Methodology: EIA

	Result	Reference Range
Zonulin Family Peptide, Stool	86.0	22.3-161.1 ng/mL

Zonulin Family Peptide

This test is for research use only. Genova will not provide support on interpreting the test results. This test does not detect zonulin.[1] The Scheffler paper suggests that the IDK kit may detect a zonulin family peptide, such as properdin. Genova's unpublished data demonstrated that the current IDK kit results were associated with stool inflammation biomarkers and an inflammation-associated dysbiosis profile.

The performance characteristics of Zonulin Family Peptide have been verified by Genova Diagnostics, Inc. The assay has not been cleared by the U.S. Food and Drug Administration.

GENOVA DIAGNOSTICS

Additional Tests

Macroscopic/Direct Exam for Parasites

Methodology: Macroscopic Evaluation

No human parasite detected in sample.

Add-on Testing

Methodology: EIA

	Result	Expected Value
HpSA - *H. pylori*	Negative	Negative
Campylobacter spp.◆	Negative	Negative
Clostridium difficile◆	Negative	Negative
Shiga toxin *E. coli*◆	Negative	Negative
Fecal Lactoferrin◆	Negative	Negative

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Key Points

- Evaluation of gut health is a key factor in all aspects of patient health
- Providing culture for bacteria and yeast detects *living* organisms, allowing for sensitivities to enhance protocol design
- Parasitology that includes a microscopic and PCR platform casts a much wider net for detection of parasites which shed unpredictably
- Genova's statistical analysis of Commensal Bacterial findings enhances pattern analysis and interpretation of findings

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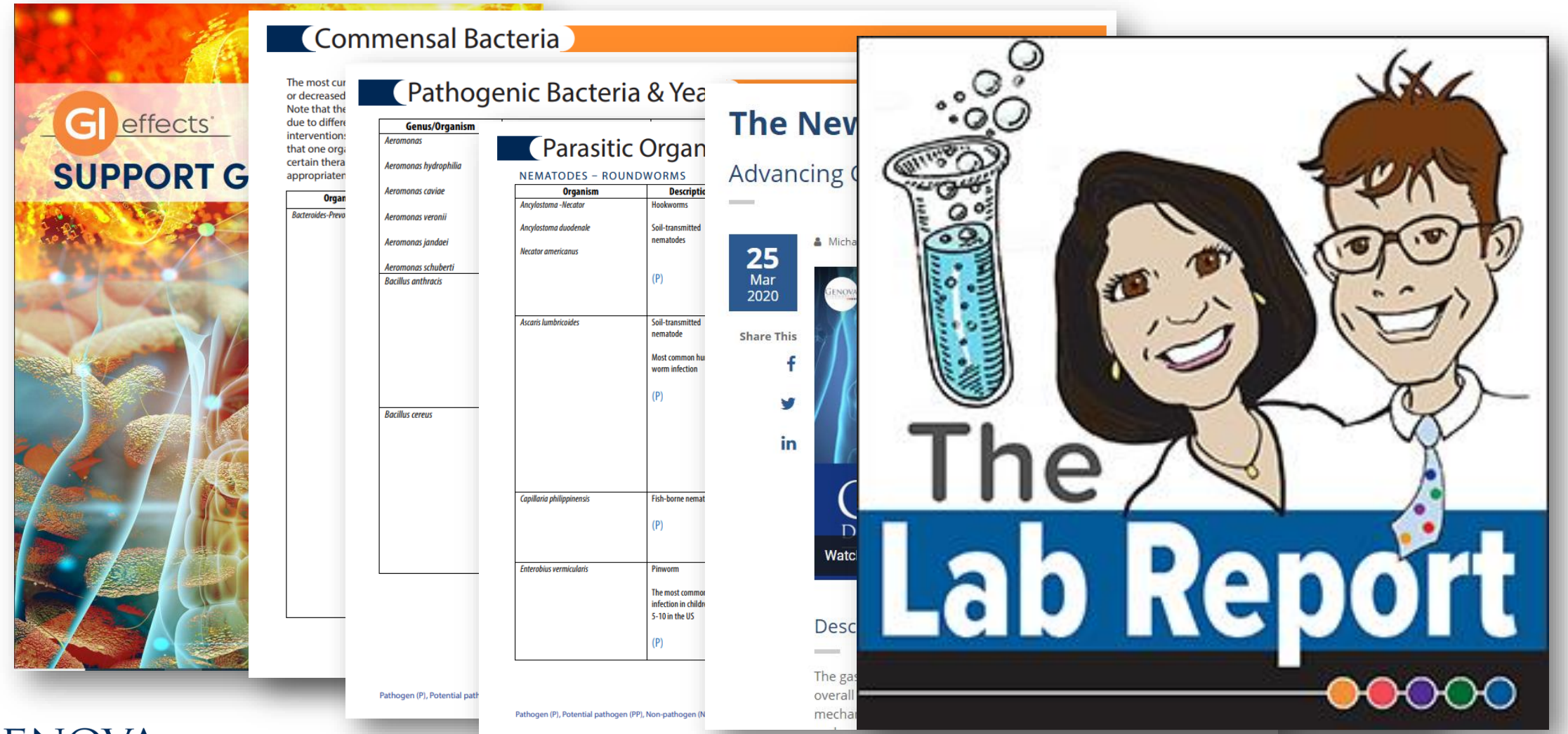
Support Materials



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